Protein aggregation and toxicity in human diseases

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Name of Fellow
Institution
Funder

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Contact information of fellow
Country

EC

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Protein aggregation and toxicity in human diseases

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The project/programme is most relevant to:

Alzheimer's disease & other dementias

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Protein aggregation | chemical kinetics | aggregation mechanism | oligomer | toxicity | abeta | Alzheimer's disease | biophysical characterization | microfluidics

Research Abstract

This research project deals with the role of protein aggregation in several human diseases which are connected to the formation of fibrillar protein structures. Currently, no effective pharmaceutical treatment is available for these diseases, a fact which reflects our present lack

of understanding of the molecular mechanism responsible for their formation and pathogenicity. This severe lack of knowledge is in large part a consequence of the lack of suitable tools to address these questions.
In this project, I propose a strategy to apply chemical kinetic analysis in combination with biophysics and biological assays to address the relationship between the mechanism of protein aggregation and its biological consequences. The study will focus on the amyloid-? peptide (A?), the peptide implicated in Alzheimer’s disease. The approach and the platform developed in this project will be also of relevance for a large number of other biological systems. I plan to build on the possibility open only recently by biophysical techniques to follow the time evolution of the concentration of the oligomers during the aggregation process and apply the chemical kinetic approach to measure the rate laws and identify the aggregation mechanism of the oligomers. In parallel, by performing kinetic experiments on toxicity I plan to apply the same strategy to identify the aggregation mechanism of the processes that generate toxicity, with the attractive prospective of improving our quantitative understanding of the mechanistic relationship between protein aggregation and its biological consequences. In a second stage of the project I plan to tackle the limitations of conventional biophysics in characterizing the oligomers by developing new biophysical tools based on microfluidic technology to allow the rapid characterization of heterogeneous samples in short time and improve the detection resolution of the oligomer population with respect to traditional approaches.

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